against a botulinum toxin, and (ii) a purification moiety that binds [adapted to bind] to a chromatography column,

(b) obtaining from said host cell an extract comprising the fusion protein,

(c) purifying the fusion protein using chromatography column,

(d) incorporating the purified fusion protein into a pharmaceutical composition.

19. (Twice Amended) A pharmaceutical composition comprising:[-]

(a) a fusion protein, said protein being a fusion of (i) a polypeptide [fee] free of toxin activity and capable of inducing protective immunity against a botulinum toxin, and (ii) a polypeptide [adapted to bind] that binds to a chromatography column; and

(b) a pharmaceutically acceptable carrier.

21. (Twice Amended) A pharmaceutical composition according to Claim 20 wherein the fusion protein comprises a polypeptide that binds [adapted to bind] to an affinity chromatography column.

REMARKS

Reconsideration is requested.

Claims 1-25 are pending. Claims 1-12 and 19-24 are active. Claims 13-18 and 25 have been withdrawn as being drawn to an allegedly separately patentable invention.

Reconsideration and withdrawal of the restriction requirement are requested in view of the following.

Claims 1-12 and 19-24 relate to a polypeptide which is free of botulinum toxin activity and toxoid which provides protective immunity to a type F botulinum toxin, derivatives, fragments, fusion proteins and compositions containing the same and methods of using the same. Claims 13-18 and 25 are directed to recombinant DNA encoding the polypeptide (claims 13 and 25), and methods of producing the polypeptide involving use of the DNA encoding at least the polypeptide, derivative, fragment or fusion protein (claims 14-18). The present application is a U.S. national phase of a PCT application designating the U.S. such that the "unity of invention (not restriction) practice is applicable". See, MPEP §1893.03 p 1800-126 (July 1998). The Examiner is urged to appreciate the following:

> "When making a lack of unity of invention requirement, the examiner must (1) list the different groups of claims and (2) explain why each group lacks unity with each other group (i.e., why there is no single general inventive concept) specifically describing the unique special technical feature in each group.
>
> The principles of unity of invention are used to determine the types of claimed subject matter and the combinations of claims to different categories of invention that are permitted to be included in a single international or national stage patent application. The basic principle is that an application should relate to only one invention or, if there is more than one invention, that applicant would have a right to include in a single application only those inventions which are so linked as to form a single general inventive concept.
>
> A group of inventions is considered linked to form a single general inventive concept where there is a technical relationship among the inventions that involves at least one common or corresponding special technical feature. The expression special technical features is defined as meaning those technical features that define the contribution which each claimed invention, considered as a whole, makes over the prior art. For example, a corresponding technical feature is exemplified by a key defined by certain claimed structural characteristics which correspond to the claimed features of a lock to be used with the claimed key. Note also examples 1-17 of Annex B Part 2 of the PCT Administrative Instructions

> as amended July 1, 1992 contained in Appendix AI of the MPEP."

The Applicants also urges the Examiner to appreciate that Example 17 of Annex B Part 2 of the PCT Administrative Instructions referred to above, indicates that a claim 1 to "Protein X" shares a common unity of invention with a claim 2 to "DNA sequence encoding protein X." (see, page AI-43 of the MPEP (July 1998)) because

> "Expression of the DNA sequence in a host cell results in the production of a protein which is determined by the DNA sequence. The protein and the DNA sequence exhibit corresponding special technical features. Unity between claims 1 and 2 is accepted." Id. (Underlined emphasis added.)

Withdrawal of the restriction requirement and examination of all the pending claims are requested.

In the event the Examiner maintains the restriction requirement after consideration of the above, the applicants request consideration of the attached Alternate Rule 181 Petition and written notification to the undersigned that the attached Alternate Rule 181 Petition is being considered.

A certified copy of the priority document is attached.

The specification has been amended to include an Abstract. The undersigned notes the Preliminary Amendment of December 12, 1997, indicates at page 3 that an Abstract has previously been submitted. The Examiner is requested to ensure the application contains one Abstract.

Claim 19 has been amended above to obviate the objection to the same stated at page 3, ¶4 of Paper No. 10. Withdrawal of the objection is requested.

Claims 1-7 and 9-10 have been amended to obviate the Section 101 rejection of the same. Withdrawal of the Section 101 rejection of claims 1-7 and 9-10 is requested.

The Section 112, first paragraph rejection of claims 3-6 is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following comments.

Initially, the applicants note the Examiner's reliance of Lazar (Mol. Cell. Bio. 8: 1247-1252 (1988)) and Burgess (J. Cell Bio. 111: 2129-2138 (1990)) is inappropriate as Lazar was published 7 years prior to the instant invention and Burgess was published 5 years prior to the present invention. The level of skill in this art has advanced in the intervening time and these documents are not representative of the level of skill in this art at the time of the present invention. More importantly, Lazar is a report of transforming growth factor α and Burgess involves studies of heparin-binding growth factor, neither of which are the subject of the presently claimed invention. Finally, neither Lazar nor Burgess reviewed the present disclosure or report on the predictability of making the presently claimed invention or the amount of experimentation required to make the presently claimed invention.

The applicants note the Examiner has objected to the term "derivative" on the grounds that the specification does not "enable" the full range of possible derivatives that might be produced without undue experimentation. It has been suggested that this term encompasses a myriad of derivatives where random peptides have been changed. This interpretation is not consistent however with the definition of this term provided in the specification on page 5, lines 8-11.

It is submitted that when the objected-to term is interpreted in view of the disclosure, the amount of experimentation necessary to arrive at a range of suitable derivatives would not be undue. The Examiner has not objected to the term "fragments" in the same way. A skilled

person would be in a position to combine immunogenic fragments in a variety of ways, and by routine biological testing, determine the level of activity of the combination, with a reasonable expectation that some activity at least, would be retained.

It would be inequitable if the applicants were not to be allowed to obtain protection for this sort of derivative structure. Accordingly, the applicants submit the claims are supported by an enabling disclosure and withdrawal of the Section 112, first paragraph rejection is requested.

The Section 112, second paragraph rejection of claims 5 and 6 stated at ¶7 of Paper No. 10 is obviated by the above amendments. The applicants note claim 5 was amended in the Preliminary Amendment of December 12, 1997, to include traditional Markush language. Claim 6 has been amended above to incorporate the language of claim 5. The use of the alternative, "or", is not contained in either claims 5 or 6 and the Examiner is requested to clarify his reference to the same in the event the rejection is maintained. The Section 112, second paragraph rejection of claims 7-12 and 19-24 is obviated by the above amendments. Withdrawal of the rejection is requested.

The Section 102 rejection of claims 1-2, 12 and 22 over Sesardic (WO 94/21684) is traversed. Reconsideration and withdrawal of the rejection is requested in view of the following distinguishing remarks.

The teaching of Sesardic is to utilize a polypeptide, which may be a region of a botulinum toxin, as an enhancer for the known type of toxoid vaccines. The toxoid vaccines mentioned are the conventional ones such as the pentavalent A-E toxoid (see, for example, claim 17).

Therefore, Sesardic does not teach the invention of the present claims. There is no teaching in Sesardic of the use of specific polypeptides for protection against specific types of

botulinum toxin. Certainly, there is nothing to point towards the use of peptides which are specific to type F toxin.

Consequently, it is not seen that this rejection is sustainable and withdrawal of the Section 102 rejection is requested.

In view of the above and attached, the claims are submitted to be in condition for allowance and a Notice to that effect is requested.

Respectfully submitted,

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